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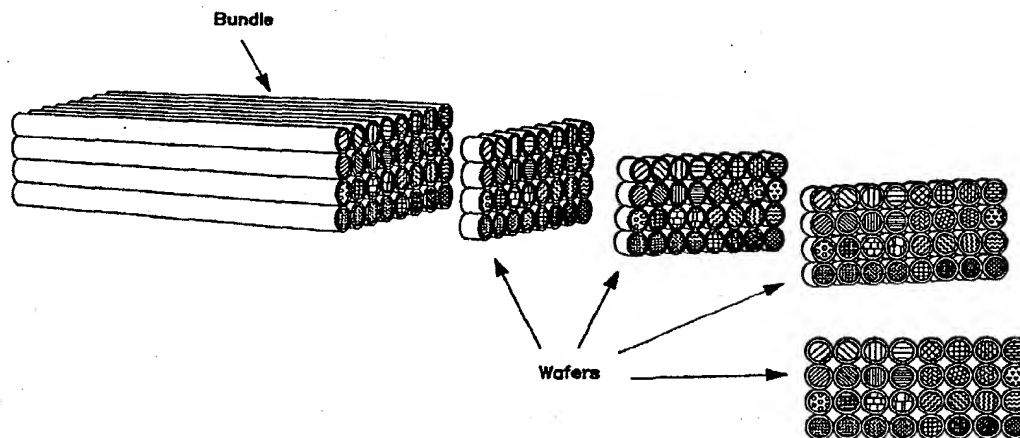
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<b>(21) International Application Number:</b> PCT/US98/21860 <b>(22) International Filing Date:</b> 16 October 1998 (16.10.98) <b>(30) Priority Data:</b> 60/062,203 16 October 1997 (16.10.97) US <b>(63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application</b> US 60/062,203 (CIP) Filed on 16 October 1997 (16.10.97) <b>(71)(72) Applicant and Inventor:</b> MILLSTEIN, Larry, S. [US/US]; P.O. Box 6196, Springfield, VA 22150-6196 (US).	<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). <b>Published</b> <i>With international search report.</i> <i>With amended claims.</i> <b>Date of publication of the amended claims:</b> 27 May 1999 (27.05.99)	

**(54) Title:** METHOD FOR PRODUCING ARRAYS AND DEVICES RELATING THERETO



**(57) Abstract**

An invention that relates to arrays, to methods and devices for producing arrays and to methods and devices for using arrays is described. In a particular aspect the invention relates to methods in which array members are aligned in a bundle and the bundle then is sectioned across the alignment to produce replicate arrays. In a further particular aspect the invention relates to arrays of analyte binding reagents. In another particular aspect the invention relates to micro-arrays.

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## AMENDED CLAIMS

[received by the International Bureau on 2 April (02.04.99);  
original claims 1-47 amended (6 pages)]

1. A method of making arrays of a plurality of array members, comprising the steps of:
  - (A) providing a plurality of bundle members, each bundle member comprising at least one array member;
  - (B) forming the bundle members into a bundle in which the array members are aligned;
  - (C) sectioning the bundle to produce wafers that comprise an array of the array members;wherein at least one array member is homogeneous.
2. A method of making arrays of a plurality of array members, comprising the steps of:
  - (A) providing a plurality of bundle members, each bundle member comprising at least one array member;
  - (B) forming the bundle members into a bundle in which the array members are aligned;
  - (C) sectioning the bundle to produce wafers that comprise an array of the array members;wherein at least one bundle member comprises an array member disposed within a structural member.
3. A method of making arrays of a plurality of array members, comprising the steps of:
  - (A) providing a plurality of bundle members, each bundle member comprising at least one array member;
  - (B) forming the bundle members into a bundle in which the array members are aligned;
  - (C) sectioning the bundle to produce wafers that comprise an array of the array members;wherein at least one bundle member comprises a homogeneous array member disposed within a structural member.

4. A method of making arrays of a plurality of array members, comprising the steps of:
- (A) providing a plurality of bundle members, each bundle member comprising at least one array member;
  - (B) forming the bundle members into a bundle in which the array members are aligned;
  - (C) sectioning the bundle to produce wafers that comprise an array of the array members;  
wherein at least one array member is acellular.
5. A method according to any of claims 1-4, wherein the array members are cross-sectioned perpendicular to their alignment.
6. A method according to any of claims 1-4, wherein the array members are cross-sectioned at an angle of 10 to 80 degrees or 100 to 170 degrees to their alignment.
7. A method according to any of the foregoing claims, wherein the array members are cross-sectioned by a smooth planar cut.
8. A method according to any of claims 1-6, wherein the array members are cross-sectioned by a non-planar cut.
9. A method according to claim 8, wherein the surface area of array members exposed by cross-sectioning is increased over that provided by a smooth, planar cut.
10. A method according to any one of claims 1-4, wherein array members are comprised of or are disposed within a plastic, a glass, a metal or a ceramic.
11. A method according to claim 10, wherein array members are comprised of or disposed within a glass.
12. A method according to claim 10, wherein array members are comprised of or disposed within a plastic.

13. A method according to claim 12, wherein the plastic is a polycarbonate, polyethylene, polymethylmethacrylate, polystyrene, a copolymer of polystyrene, polysulfone, polyvinylchloride, polyester, polyamide, polyacetal, polyethyleneterephthalate, polytetrafluoroethylene or polyurethane.

14. A method according to claim 13, wherein the plastic is a polycarbonate, polyethylene, polystyrene, a copolymer of polystyrene, polysulfone or polyvinylchloride.

15. A method according to any one of claims 1-4, wherein the array members are spaced about 1.0 to about 1,000 micrometers apart.

16. A method according to any one of claims 1-4, wherein the array members have a cross-sectional area of about 1.0 to about 1,000,000  $\mu\text{m}^2$ .

17. A method according to any one of claims 1-4, wherein the density of array members in the array is about 250 to about 2,500,000 array members per square centimeter of cross sectional surface area of the array.

18. A method according to any one of claims 1-4, wherein the density in the array is about 10 to about 100,000 array members per square centimeter of total surface area at the array.

19. A method according to any one of claims 1-4, wherein there are about 100 to about 2,500,000 aligned array members.

20. A method according to any one of claims 1-4, wherein there are about 100 to 2,500,000 different aligned array members.

21. A method according to any one of claims 1-4, wherein cross-sectioning produces sections about 2.5 to about 2,500 micrometers thick.

22. A method according to any one of claims 1-4, wherein at least two array members are different from one another.

23. A method according to any one of claims 1-4, wherein (C) comprises repeatedly cross-sectioning a plurality of aligned array members to produce sections with at least one surface that exposes array members in the same disposition, thereby replicating the array.

24. A method according to any one of claims 1-4, wherein the array members comprise analyte binding reagents.

25. A method according to claim 24, wherein the array comprises analyte binding reagents that hybridize to DNA or RNA having specific nucleotide sequences.

26. A method according to claim 25, wherein the sequence specific binding reagents are polynucleotides, peptide-nucleic acids or polyamides.

27. A method according to claim 26, wherein the sequence specific binding reagents are oligonucleotides.

28. A method according to claim 24, wherein the array comprises analyte binding reagents that bind specific polypeptides.

29. A method according to claim 28, wherein the polypeptide-specific binding reagents are polyclonal antibodies, monoclonal antibodies, a single chain antibody, or an antigen-binding fragment of an antibody.

30. A method according to claim 24, wherein analyte binding reagents are one or more of a nucleic acid, a polynucleotide, a DNA, an RNA, an oligonucleotide, a protein-nucleic acid, an aptamer, a ribozyme, a nucleic acid-binding polyamide, a protein, a peptide, a polypeptide, a glycoprotein, an antibody, an antibody-derived polypeptide, a receptor protein, a fusion protein, a mutin, a lipid, a polysaccharide, a lectin, a ligand, an antigen or a hapten.

31. A method according to claim 24, wherein the array is used to carry out an immunoassay, a hybridization assay, a ligand-binding assay or receptor-binding assay, or a substrate analog affinity assay.

32. A method according to claim 24, wherein binding to the analyte binding reagents is detected using radioactivity, fluorescence, phosphorescence or chemiluminescence.

33. A wafer comprising a plurality of array members in an array, wherein at least one array member is homogeneous, forms part of two opposing surfaces of the wafer and extends uniformly between the two surfaces.

34. A wafer comprising a plurality of array members in an array, wherein each array member is homogeneous, forms part of two opposing surfaces of the wafer and extends uniformly between the two surfaces.

35. A wafer comprising a plurality of array members in an array, wherein at least one array member is homogeneous and disposed within a structural member, forms part of two opposing surfaces of the wafer and extends within the structural member uniformly between the two surfaces.

36. A wafer comprising a plurality of array members in an array, wherein each array member is homogeneous and disposed within a structural member, forms part of two opposing surfaces of the wafer and extends within the structural member uniformly between the two surfaces.

37. A wafer comprising a plurality of array members in an array for performing chemical, biochemical or biological assays, wherein at least one array member is an analyte binding reagent, is homogeneous, forms part of two opposing surfaces of the wafer and extends uniformly between the two surfaces.

38. A wafer comprising a plurality of array members in an array for performing chemical, biochemical or biological assays, wherein each array member is an analyte binding reagent, is homogeneous, forms part of two opposing surfaces of the wafer and extends uniformly between the two surfaces.

39. A wafer according to any of claims 33-38, wherein the array members are spaced about 1.0 to about 1,000 micrometers apart.

40. A wafer according to any of claims 33-38, wherein the array members have a cross-sectional area of about 1.0 to about 1,000,000  $\mu\text{m}^2$ .

41. A wafer according to any of claims 33-38, wherein the density of array members in the array is about 250 to about 2,500,000 array members per square centimeter of cross sectional surface area of the array.

42. A wafer according to any of claims 33-38, wherein the density in the array is about 10 to about 100,000 array members per square centimeter of total surface area of the array.

43. A wafer according to any of claims 33-38, wherein there are about 100 to about 2,500,000 array members in the array.

44. A wafer according to any of claims 33-38, wherein there are about 100 to 2,500,000 different array members in the array.

45. A wafer according to any of claims 33-38, wherein cross-sectioning produces sections about 2.5 to about 2,500 micrometers thick.

46. A wafer according to any of claims 33-38, wherein the array comprises analyte binding reagents that hybridize to DNA or RNA having specific nucleotide sequences.

47. A wafer according to any of claims 33-38, wherein the array comprises analyte binding reagents that bind specific polypeptides.